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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/715,143	11/17/2003	Rajiv Shah	047711-0325	1899

23392 7590 06/23/2006

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EXAMINER

PAK, YONG D

ART UNIT PAPER NUMBER

1652

DATE MAILED: 06/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/715,143

Applicant(s)

SHAH ET AL.

Examiner

Yong D. Pak

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 November 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) 18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 17 November 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>11/17/03</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This application is a divisional of 10//035,918.

Claims 1-18 are pending and are under consideration.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 1-17, drawn to a method of formulating a glucose oxidase, classified in class 435, subclass 71.1.
- II. Claim 18, drawn to a glucose oxidase, classified in class 435, subclass 189.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make another and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the glucose oxidase of Invention I can be isolated from a microorganism. Searching the inventions of I-II together would impose serious search burden. The inventions of groups I-II have a separate status in the art as shown by their different classifications. Moreover, even if the polypeptide product were known, the methods of group II may be novel and unobvious in the view of the preamble or active steps.

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Because these inventions are distinct for the reasons given above and the search required for Group I not required for II, restriction for examination purposes as indicated is proper.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and recognized divergent subject matter, restriction for examination purposes as indicated is proper.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

During a telephone conversation with Mr. Rittmaster on June 14, 2006, a provisional election was made with traverse to prosecute the invention of Group I, claims 1-17. Affirmation of this election must be made by applicant in replying to this Office action. Claim 18 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

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In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on November 17, 2003 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Drawings

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

Claim Objections

Claim 2 is objected to because the name of the organisms recited in the claim should be italicized.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4 and 6 and claim 5 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4 and 6 recite the phrase "identify colonies with active glucose oxidase". It is not clear to the Examiner as to how those skilled in the art can conclude that colonies have active glucose oxidase by only measuring fluorescence or by using a substance that changes color in the presence of active glucose oxidase. This is because in the claimed method, applicants have not set up any control steps. Therefore, the method lacks essential step(s). Examiner requests clarification of the claimed method.

Claims 7-10 and claims 11-18 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 7-10 recite the term "functionality". The metes and bounds of this term in the context of the above claims are not clear to the Examiner. A perusal of the specification did not provide the Examiner with a specific definition for the above term. Therefore, it is not clear to the Examiner either from the specification or from the claim

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as to what specific "functions" of glucose oxidases are encompassed in the term "functionalities". Examiner requests clarification of the above term.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3 and 7-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Valdes et al., Hatzinikolaou et al. and Stemmer.

Claims 1-3 and 7-8 are drawn to a method of formulating glucose oxidases by obtaining an organism, such as an *E. coli*, with glucose oxidase genes, growing

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colonies of the organism, altering the environment of the colonies, such as introducing peroxide, screening the colonies to identify colonies with active glucose oxidase and determining whether the colonies grown in the presence of peroxide are active.

Valdes et al. (form PTO-892) discloses that glucose oxidase in glucose sensors are degraded by peroxide and this "decay can lead to the eventual failure of the sensor" (abstract and page 367). Valdes et al. teaches that to ensure longer sensor functionality, instead of replacing the sensor with fresh enzyme, as has been practiced in the art, techniques to "prevent the degradation of the enzyme" is advantageous (page 375). With this teaching at hand, one having ordinary skill in the art would have concluded that degradation of glucose oxidase in a sensor may be prevented by using chemical agents, as suggested by Valdes et al., or to use glucose oxidase mutants that are resistant to peroxide degradation, since methods of generating mutants having resistance to chemicals are known in the art, as discussed below. Valdes et al. also teaches a method of determining activity of glucose oxidase (page 370).

The difference between the reference of Valdes et al. and the instant invention is that the reference of Valdes et al. does not teach a method of producing and formulating active glucose oxidase from colonies grown in the presence of peroxide. However, there are many methods widely available in the art of creating mutant genes and screening for mutants displaying desired functional properties, such as having resistance to a chemical, such as a peroxide.

Hatzinikolaou et al. (form PTO-892) discloses a library of glucose oxidase genes known in the art, such as *A. Niger* (page 371).

Stemmer (US Patent 6,117,679 – form PTO-892) discloses a method of producing mutant enzymes by obtaining a library of genes of interest, creating a library of mutated genes by multiple cycles (at least 2-6 cycles) of PCR, error-prone PCR and/or gene shuffling (abstract, Column 4-11 and Column 22). In the method of Stemmer, each mutated genes are introduced into separate expression vectors, which are then inserted into *E. coli* (Column 25, 31-32). Stemmer teaches these host cells are then tested for the presence of desired mutations, such as growing the cells or colony under selective pressure and isolating the protein and testing of the protein encoded for activity (Column 32). Stemmer teaches a method of screening for colonies having resistance to a chemical by plating transformed cells comprising mutated genes onto agar plates having varying concentrations of said chemical (Column 78).

Therefore, combining the teachings of Valdes et al., Hatzinikolaou et al. and Stemmer, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to formulate or produce glucose oxidases having resistance to peroxide by generating a library of mutated genes using the glucose oxidase gene of Hatzinikolaou et al. and the method of Stemmer, transforming *E. coli* with vectors comprising each of the mutated genes, growing colonies of said cells in the presence of peroxide and determining whether the colonies have active glucose oxidase. One of ordinary skill in the art would have been motivated to do so in order to generate active glucose oxidases that are resistant to peroxide. One of ordinary skill in the art would have been motivated to produce mutant peroxide resistant glucose oxidases in order to use them in glucose sensors, thereby prolonging their use, since

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Valdes et al. teaches that glucose oxidases in glucose sensors are degraded by peroxide, leading to failure of the sensor. One of ordinary skill in the art would have had a reasonable expectation of success since Hatzinikolaou et al. teaches glucose oxidase genes and Stemmer teaches a method of generating a library of mutant genes and screening for activity and other desired properties, such as resistance to a chemical.

Therefore, the above references render claims 1-3 and 7-8 *prima facie* obvious.

Claims 4-6 and 9-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Valdes et al., Stemmer and Hatzinikolaou et al. as applied to claims 1-3 and 7-8 above, and further in view of Wagner and Aldrich Catalog.

Claims 4-6 and 9-17 are drawn to a method of formulating or producing glucose oxidases an organism, such as an *E. coli*, with glucose oxidase genes, growing colonies of the organism, altering the environment of the colonies, such as introducing peroxide, screening the colonies to identify colonies with active glucose oxidase and determining whether the colonies grown in the presence of peroxide are active by testing glucose oxidase in sensors and using fluorescence of a leuco-cryalsta-violet.

Valdes et al., Stemmer and Hatzinikolaou et al. in combination teach a method of formulating or producing mutant glucose oxidases, as discussed above. Hatzinikolaou et al. also discloses a method of isolating and purifying glucose oxidase as recited in the claims and methods of measuring glucose oxidase activity (pages 372-373).

The difference between the reference of Valdes et al., Stemmer and Hatzinikolaou et al. and the instant invention is that said references do not teach a method of determining whether the colonies contain active glucose oxidase by testing glucose oxidase in sensors and using fluorescence.

Wagner (EP 0 251 475 A1 - form PTO-892) discloses a method of determining glucose oxidase activity via a sensor by measuring fluorescence emission from a dye, wherein oxidation of glucose by active glucose oxidase reduces the fluorescence emission (pages 2-3). In the method of Wagner, the glucose oxidase is conjugated to a dye and immobilized in the sensor (page 3). Wagner also teaches that any fluorescent dye sensitive to quenching of its fluorescence emission by oxygen can be used (page 5). Aldrich Catalog (form PTO-892) discloses a leuco-cryalsta-violet dye (page 1005).

Therefore, combining the teachings of Valdes et al., Stemmer and Hatzinikolaou et al., Wagner and Aldrich Catalog, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to use the method of Wagner to ascertain activity of the glucose oxidase, wherein glucose oxidase is isolated and purified by the method taught by Hatzinikolaou et al. One of ordinary skill in the art would have been motivated to do so in order to determine whether the colonies comprising mutated glucose oxidases have active glucose oxidase. One of ordinary skill in the art would have had a reasonable expectation of success since Wagner teaches how to determine activity of glucose oxidase by measuring fluorescence emission from a dye, wherein oxidation of glucose by active glucose oxidase reduces the fluorescence emission.

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Therefore, the above references render claims 4-6 and 9-17 *prima facie* obvious.

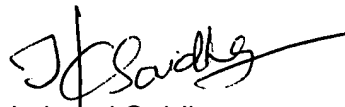
None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak
Patent Examiner 1652



Tekchand Saidha
Primary Patent Examiner 1652